Article

Influence of Billroth II Combined With Braun Anastomosis on Perioperative Stress Indicators and Pepsinogens in Patients Undergoing Laparoscopic Gastric Cancer Surgery

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AIM: The study aimed to investigate the influence of Billroth II combined with Braun anastomosis on perioperative stress indicators and pepsinogens in patients undergoing laparoscopic gastric cancer surgery.
METHODS: This study is a single-center retrospective research design. This study included 148 patients who underwent laparoscopic radical distal gastrectomy for gastric cancer between March 2021 and June 2024, with all surgical procedures performed by the same surgical team. According to the digestive tract reconstruction methods, participants were divided into a Billroth II group (n = 63) and a Billroth II+Braun group (n = 85). The short-term efficacy outcomes included perioperative stress indicators, pepsinogen I to pepsinogen II ratio (PGR), Gastrin-17 (G-17), and postoperative complications. Moreover, the long-term efficacy outcomes comprised bile reflux rate, incidence rate of reflux residual gastritis and 1-year survival rate.
RESULTS: The C-reactive protein (CRP) showed a gradual increase preoperatively (T0) and at postoperative day 1 (T1) and day 2 (T2) ($F_{\text{interaction}}$ = 2.74, p = 0.064; $F_{\text{time-point}}$ = 757.8, $p < 0.001$; $F_{\text{between-group}}$ = 2.50, p = 0.114). However, norepinephrine (NE) and cortisol (COR) initially increased and then declined at these time points ($F_{\text{interaction}}$ = 0.90, 0.58, p = 0.407, 0.559; $F_{\text{time-point}}$ = 1628, 466.4, both p < 0.001; $F_{\text{between-group}}$ = 0.83, 0.70, p = 0.36, 0.40). Furthermore, no statistical differences in CRP, NE and COR were observed between the Billroth II+Braun group and the Billroth II group at the three time points ($p > 0.05$). Compared with preoperative levels (T0), PGR increased in both groups, whereas G-17 decreased at postoperative day 30 (T3) ($p < 0.01$). Additionally, PGR was significantly higher in Billroth II+Braun group ($p < 0.001$) while there was no statistical difference in G-17 between the two groups at T3 (p = 0.943). Similarly, the anastomotic leakage (Fisher's exact test, p = 0.312), anastomotic stenosis (Fisher's exact test, p = 1.000), duodenal stump bleeding (Fisher's exact test, p = 0.426), duodenal stump leakage (Fisher's exact test, p = 0.180), and intestinal obstruction rate (Fisher's exact test, p = 0.402) also showed no statistical differences between the two groups. The bile reflux rate was substantially lower in the Billroth II+Braun group (p = 0.005), while no statistical differences were observed in residual food (p = 0.097), reflux residual gastritis (Fisher's exact test, p = 0.312) and survival rate (Fisher's exact test, p = 0.700) between groups.
CONCLUSIONS: This study demonstrates that Billroth II+Braun anastomosis and Billroth II anastomosis are equally safe and effective during radical distal gastrectomy for gastric cancer. There is no significant difference in the influence of two digestive tract reconstruction methods on perioperative stress indicators in this cohort. Additionally, Billroth II+Braun anastomosis can improve PGR level and reduce bile reflux rate.

Keywords: Billroth II; Braun anastomosis; laparoscopic radical distal gastrectomy for gastric cancer; PGI/PGII ratio

Introduction

Gastric cancer is a common malignant tumor of the digestive system and continues to impose a significant global health concern, with persistently high rates of morbidity and mortality. According to data released in 2022, newly diagnosed gastric cancer cases account for about 5.6% of all cancer cases, while deaths from gastric cancer represent 7.7% of total cancer-related deaths each year [1].Recent estimates indicate that China reports approximately 478,000 new cases and 375,000 deaths each year, accounting for 43.9% of global new cases and 48.6% of gastric cancer-related deaths, respectively [2]. A 2025 global evaluation of the survival burden of preventable gastric cancer across 185 countries reported that among individuals born between 2008 and 2017, about 15.6 million cases are expected to occur over their lifetimes. Asia is the primary source of expected burden, with more than 10.6 million cases (68%), followed by the Americas (13%), Africa (11%), Europe (8%) and Oceania (0.4%) [3].

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In China, inconsistencies in economic and healthcare resources at the primary care level limit access to early detection services. The routine use of gastroscopy remains insufficient, and public awareness about gastric cancer prevention and early diagnosis is relatively low. Additionally, the clinical manifestations and signs of early gastric cancer are not obvious, which can be easily mistaken for benign gastrointestinal conditions. Hence, many patients are diagnosed at advanced stages. The clinical staging and timing of intervention are closely correlated with therapeutic efficacy, postoperative complication rates, and long-term quality of life [4].

Although the etiology of gastric cancer has not been completely elucidated, numerous studies suggest that its development is multifactorial. *Helicobacter pylori* (Hp) infection is the principal risk factor; however, not all infected individuals ultimately develop malignancy [5]. Additional contributors include smoking, alcohol consumption, and unhealthy eating habits. While some specific factors, such as gender and age, cannot be intervened, modifiable risks can be addressed through measures such as anti-Hp therapy and lifestyle modification, thereby reducing disease occurrence. Currently, surgical intervention is the critical option for gastric cancer treatment, supplemented by comprehensive approaches including radiotherapy, chemotherapy, molecular targeted therapy, and immunotherapy. In China, lower (distal) gastric cancer is relatively common, with lesions often located along the lesser curvature of the gastric antrum, making radical distal gastrectomy a preferred primary surgical approach [6].

Reconstruction of the digestive tract after gastrectomy is usually conducted using Billroth I, Billroth II, or Roux-en-Y anastomosis [7]. Billroth I anastomosis was the earliest method used in distal gastrectomy, which preserves the anatomical structure, with a relatively lower rate of postoperative complications. However, its application depends largely on tumor location, size and clinical stage [8]. Moreover, Billroth I anastomosis may also be associated with risks such as alkaline reflux and excessive anastomotic tension, potentially causing anastomositis, bleeding, or even leakage.

Billroth II anastomosis effectively addresses the problem of excessive anastomotic tension; however, changes of the normal physiological and anatomical structure may lead to complications such as duodenal stump leakage [9].In contrast, to reduce bile reflux, Billroth II is often combined with the Braun anastomosis. Roux-en-Y anastomosis also eliminates anastomotic tension and can effectively prevent the occurrence of bile reflux and anastomotic stenosis, thereby reducing the risk of residual gastritis, reflux esophagitis, and residual gastric cancer. However, Roux-en-Y stasis syndrome (RSS) remains a potential postoperative complication, and the procedure requires high technical expertise, which can restrict its widespread adoption, particularly in primary or resource-limited hospitals.

Although Billroth II combined with the Braun anastomosis has been widely adopted, its long-term efficacy in preventing alkaline digestive juice reflux remains debated, and further clinical validation is required to elucidate its potential advantages [10,11]. In view of these ongoing controversies, the current study aims to assess the clinical efficacy of Billroth II combined with Braun anastomosis during laparoscopic radical distal gastrectomy for gastric cancer, to provide a safer and more effective method for digestive tract reconstruction.

Methods

Study Subjects and Experimental Design

This study enrolled 148 patients who received laparoscopic radical distal gastrectomy for gastric cancer at The Second Affiliated Hospital of Jiaxing University between March 2021 and June 2024, with all procedures conducted by the same surgical team to minimize variability. Based on digestive tract reconstruction methods, study subjects were categorized into the Billroth II group (n = 63) and the Billroth II+Braun group (n = 85).

Inclusion criteria for patient selection were as follows: (1) age between 18 and 85 years; (2) postoperative pathological confirmation of primary gastric cancer, with pathological stage I–III; (3) undergoing Laparoscopic distal gastrectomy with Dissection 2 (D2) lymph node dissection with either Billroth II anastomosis or Billroth II combined with the Braun anastomosis; (4) no preoperative adjuvant therapy; and (5) availability of complete clinicopathological data.

Exclusion criteria included (1) postoperative pathology indicating benign tumors or secondary gastric lesions; (2) substantial major organ dysfunctions, including cardiac, pulmonary, or renal impairment; (3) coagulation abnormalities; (4) diagnosis of concurrent malignant tumors; (5) severe preoperative chronic underlying diseases, with American Society of Anesthesiologists (ASA) grade >3; and (6) severe preoperative malnutrition: Nutrition Risk Screening 2002 (NRS2002) nutritional score >5 points or serum albumin level <30 g/L [12]. This definition draws on previous clinical studies to identify individuals at high risk of malnutrition. A flowchart of the patient selection process is shown in Fig. 1.

This study was approved by the medical ethics committee of The Second Affiliated Hospital of Jiaxing University (Approval No. 2025-019). Informed consent was obtained from all patients, and the study was conducted in accordance with the principles of the Declaration of Helsinki. Data confidentiality was maintained by the research team and the data were only used for academic publication and ethical review (avoiding any commercial use of the data). Patient data and information were anonymized throughout data recording and analysis to ensure no infringement of personal privacy. We ensure the safety of the patients, as the participants in this study were not exposed to additional risk. The grouping conditions and study processes or pro-

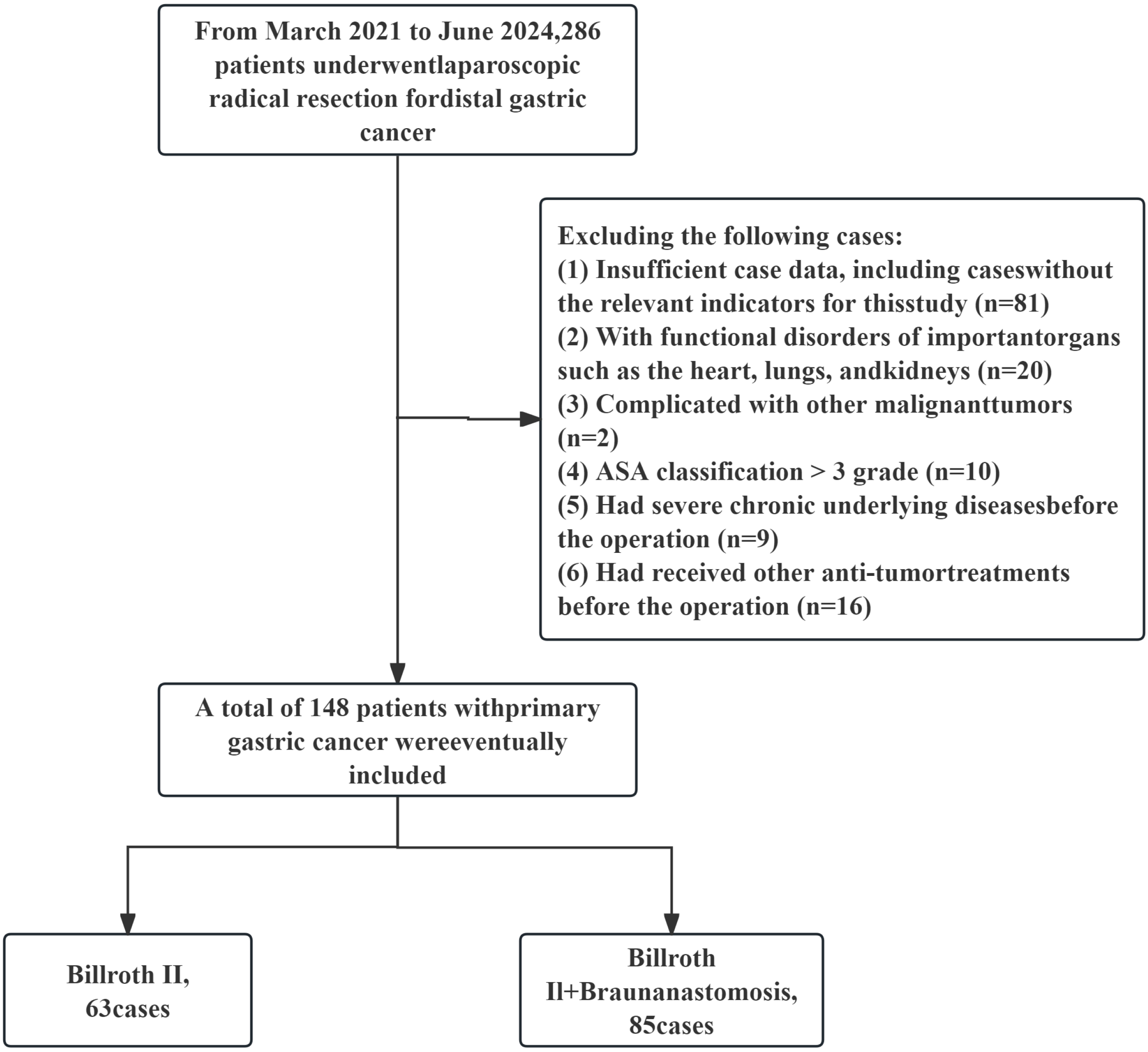

Fig. 1. A flowchart of patient selection and study design. ASA, American Society of Anesthesiologists.

cedures did not affect the original treatment regimens or influence clinical outcomes.

Treatment Protocols

The surgical equipment and instruments used in this study included a Johnson & Johnson (New Brunswick, NJ, USA) EECHELON^{TM} 3000 60mm stapler, OLYMPUS-UHI-4 insufflator, OLYMPUS-OTV-S190 laparoscope system, GEN11 ultrasonic scalpel system, OLYMPUS-CLV-S190 light source, and OLYMPUS-ESG-400 electric scalpel.

All participants underwent comprehensive preoperative evaluation in strict accordance with standardized surgical procedures. For patients with gastric retention, appropriate perioperative preparation was performed, including gastrointestinal decompression, gastric tube indwelling, gastric cavity irrigation with hypertonic warm saline to reduce gastric wall edema, preoperative optimization of blood pressure and blood glucose levels, correction of anemia, and nutritional support to improve patients' nutritional status. Informed consent was obtained after a detailed discussion with patients and their family members about the purpose, methods, risks and potential outcomes of surgery.

General anesthesia and tracheal intubation were performed, and the patients were placed in a supine and split-leg position. Appropriate intraoperative positioning was adjusted as needed. In addition, the 5-port laparoscopic method was adopted, with trocar placement tailored to the patient's body shape and the surgeon's preference to avoid instrument interference. The laparoscope holder stood between the patient's legs to provide a clear operative field. The surgeon and assistant were positioned on either side. Both anterior and posterior approaches were used as required, and the surgeon flexibly adjusted the position and selected the appropriate surgical pathway according to intraoperative findings and technical considerations. A detailed exploration of the abdominal and pelvic cavities was performed to exclude metastatic lesions and to evaluate the overall tumor condition before laparoscopic radical distal gastrectomy. Initially, the stomach was mobilized and the tumor was excised, and then the lymph node was dissected in accordance with the Japanese Gastric Cancer Treatment Guidelines, specifically D2 lymph node [13]. Subsequently, digestive tract reconstruction was implemented according to group allocation.

In the Billroth II group, the duodenum was dissected using a linear stapler approximately 2 cm from the lower edge of the pylorus, and the stomach was resected about 5 cm proximal to the tumor. The stump stomach was reinforced, and the duodenal stump was sutured and embedded with absorbable sutures. A segment of the jejunum approximately 20–30 cm distal to the Treitz ligament is selected as the anastomosis site. Subsequently, the gastrojejunal anastomosis was performed between the residual gastric posterior wall and the jejunum. Finally, the common anatomy was closed with a continuous 3-0 barbed suture. The potential gap (Petersen's defect) between mesojejunum and transverse mesocolon was closed by routine suture, and the jejunal input loop and output loop were examined to ensure no torsion.

In the Billroth II+Braun group, the duodenum and stomach were transected using a linear cutting closure about 2 cm from the lower edge of the pylorus and approximately 5 cm above the tumor. The stump stomach was reinforced, and the duodenal stump was sutured and embedded with absorbable suture. A segment of the jejunum approximately 20–30 cm distal to the Treitz ligament is selected as the anastomosis site. Then, the gastrojejunal anastomosis was implemented with the residual gastric posterior wall. The common anastomotic orifice was closed using a continuous 3-0 barbed suture. A side-to-side jejuno-jejunal anastomosis (Braun anastomosis) is performed between the input and output loops, approximately 10–15 cm distal to the gastrojejunal anastomosis. Similarly, all mesenteric defects were routinely closed to reduce the risk of internal herniation.

Data Collection

We collected and analyzed various parameters as follows:

(1) Baseline characteristics included gender, age, body mass index (BMI), presence of hypertension or diabetes mellitus, maximum tumor diameter, ASA grading, Lauren histological classification, tumor location, and Tumor Node Metastasis (TNM) staging.

(2) Intraoperative variables included the number of lymph nodes dissected and total surgical time.

(3) Short-term efficacy outcomes comprised perioperative stress indicators, gastrointestinal functional markers, and postoperative complications. Perioperative stress was determined by assessing serum cortisol (COR), norepinephrine (NE) and C-reactive protein (CRP) preoperatively (T0), at postoperative day 1 (T1), and postoperative day 2 (T2). Gastrointestinal function was assessed using the pepsinogen I to pepsinogen II ratio (PGR) and Gastrin-17 (G-17), determined preoperatively (T0) and at postoperative day 30 (T3). Postoperative complications encompassed anastomotic leakage, anastomotic stenosis, duodenal stump bleeding, duodenal stump leakage, and intestinal obstruction.

(4) Long-term efficacy outcomes included incidence of bile reflux, occurrence of reflux-related residual gastritis, and 1-year survival rate.

Evaluation Criteria and Follow-Up

Patients were followed up via outpatient visits and telephone interviews for a duration of 1 year after surgery. The patients were followed up once a month for the first 3 months and then once every 3 months, with a 1-year follow-up in total. Survival status was documented throughout the follow-up period. At 1 year after surgery, gastroscopy was re-performed, and the condition of the residual stomach and gastrojejunal anastomosis was assessed using the Japanese Residue, Gastritis, Bile (RGB) scoring system, which evaluates residual food, gastritis, and bile reflux. The Japanese RGB scoring criteria were defined as follows: residual food (0 points: no residual food; 1 point: minimal residual food; 2 points: moderate residual food, with entire residual gastric surface observable after body repositioning; 3 points: moderate residual food, with incomplete surface observation despite body repositioning; 4 points: extensive residual food, preventing adequate endoscopic observation), residual gastritis (0 points: normal residual gastric mucosa; 1 point: mild redness of residual gastric mucosa; 2 points: intermediate findings between mild and severe conditions (such as between 1 point and 3 points); 3 points: severe mucosal erythema (redness); 4 points: erosion of residual gastric mucosa), and bile reflux (0 points: no bile reflux; 1 point: presence of bile reflux) [14]. The scores of Residual food, Gastritis and Bile reflux were recorded respectively. The score of each item $\geq$1 indicated the presence of the symptom. All endoscopic assessments were performed by the same endoscopist to ensure consistency in evaluation.

Statistical Analysis

Data analysis was conducted using SPSS version 27.0 (SPSS Inc., Chicago, IL, USA). Normality of the data was assessed using the Shapiro-Wilk test. A p-value ≥ 0.05 suggested that the data met the normality requirement, whereas a p-value < 0.05 indicated a significant deviation from the normal distribution. Categorical variables were reported as numbers and percentages [n (%)] and analyzed using the chi-square test or Fisher's exact test, as appropriate. Normally distributed measurement data or variables were expressed as mean $\pm$ standard deviation (SD), and com-

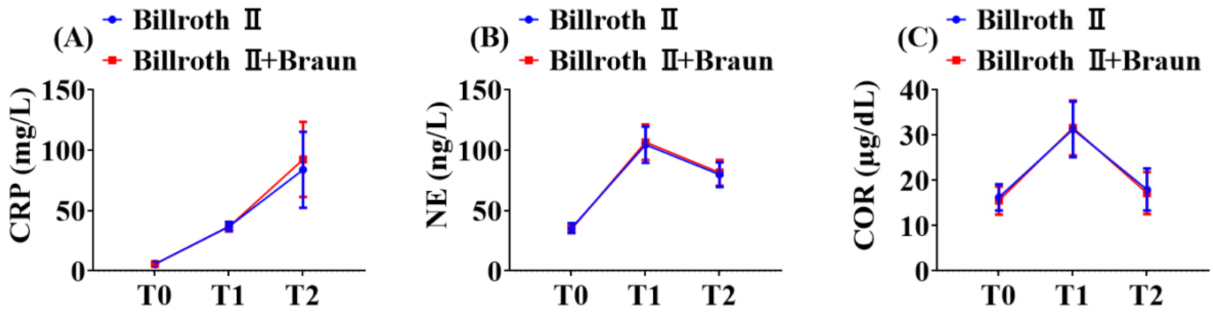

Fig. 2. Changes in perioperative stress indicators were assessed at three time points. (A) CRP. (B) NE. (C) COR. T0: preoperatively; T1: at postoperative day 1; T2: at postoperative day 2. CRP, C-reactive protein; NE, norepinephrine; COR, cortisol.

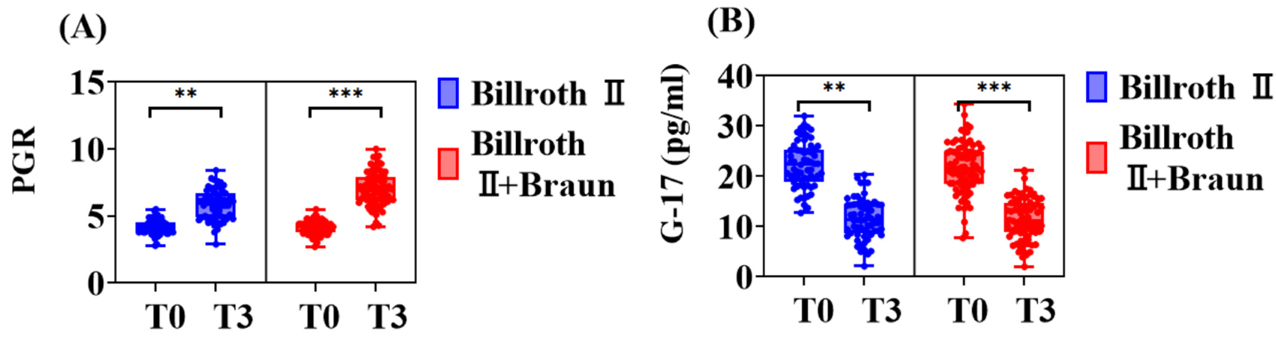

Fig. 3. Changes in PGR and G-17 levels between groups. (A) PGR. (B) G-17. T0: preoperatively; T3: at postoperative day 30; **$p < 0.01$, ***$p < 0.001$. PGR, pepsinogen I to pepsinogen II ratio; G-17, Gastrin-17.

parison between groups was performed using the independent sample t-test. Data consistent with skewed distribution were reported as median with interquartile range [M (Q_1, Q_3)] and analyzed using the Mann-Whitney U test. Additionally, repeated measures analysis of variance (ANOVA) was utilized for variables measured at multiple time points. A significance level was considered as $\alpha = 0.05$. When the p-value is less than 0.05, it is considered to have a significant difference.

Results

Comparison of Demographic Characteristics Between the Two Groups

This study included 148 patients, comprising 63 cases in the Billroth II group and 85 cases in the Billroth II+Braun group. As summarized in Table 1, the baseline characteristics were comparable between the two groups. There were no statistical differences between the two groups in terms of age ($p = 0.821$), BMI ($p = 0.509$), number of lymph nodes dissected ($p = 0.295$), maximum tumor diameter ($p = 0.887$), surgical time ($p = 0.084$), gender distribution ($p = 0.955$), prevalence of hypertension ($p = 0.750$) or diabetes mellitus ($p = 0.827$), ASA grading ($p = 0.500$), Lauren histological classification ($p = 0.906$), tumor location (Fisher's exact test, $p = 0.277$), and TNM stage ($p = 0.765$).

Comparison of Perioperative Stress Indicators Between Groups

Mauchly's sphericity test was performed for CRP, NE and COR assessed at three time points in the two groups. The findings (CRP: $p = 0.137$, NE: $p = 0.224$, and COR: $p = 0.129$) indicated that the assumption of sphericity was not violated. As shown in Fig. 2, CRP levels exhibited a gradual increase from T0 to T1 and T2 ($F_{\text{interaction}} = 2.74$, $p = 0.064$; $F_{\text{time-point}} = 757.8$, $p < 0.001$; $F_{\text{between-group}} = 2.50$, $p = 0.114$). However, NE and COR levels were elevated initially and then reduced over the same time points ($F_{\text{interaction}} = 0.90, 0.58$, $p = 0.407, 0.559$; $F_{\text{time-point}} = 1628, 466.4$, both $p < 0.001$; $F_{\text{between-group}} = 0.83, 0.70$, $p = 0.36, 0.40$).

As summarized in Table 2, the CRP, NE and COR demonstrated no statistical differences between the Billroth II+Braun group and the Billroth II group at any of the assessed time points ($p > 0.05$), indicating that the addition of the Braun anastomosis does not increase perioperative stress response in patients receiving laparoscopic gastric cancer surgery.

Comparison of PGR and G-17 Levels Between Groups

As illustrated in Fig. 3, both groups showed a substantial increase in PGR and a significant decrease in G-17 at T3 compared with preoperative levels ($p < 0.01$). Between-group comparison (Table 3) demonstrated that the Billroth

Table 1. Comparison of demographic characteristics between the two groups.

Variable	Total (n = 148)	Billroth II (n = 63)	Billroth II+Braun (n = 85)	Statistic	p-value
Age, Mean ± SD, years	61.51 ± 10.49	61.29 ± 10.21	61.68 ± 10.76	t = –0.23	0.821
BMI, Mean ± SD, kg/m^2	22.02 ± 2.55	22.19 ± 2.36	21.90 ± 2.69	t = 0.66	0.509
Number of lymph nodes dissected, Mean ± SD, nodes	32.91 ± 3.65	32.54 ± 3.59	33.18 ± 3.69	t = –1.05	0.295
Maximum tumor diameter, M (Q_1, Q_3), cm	2.90 (2.50, 3.40)	2.90 (2.50, 3.40)	2.90 (2.50, 3.40)	Z = –0.14	0.887
Surgical time, M (Q_1, Q_3), min	155.00 (135.00, 169.25)	153.00 (130.00, 164.00)	158.00 (138.00, 171.00)	Z = –1.73	0.084
Gender, n (%)				χ^2 = 0.00	0.955
Female	45 (30.41)	19 (30.16)	26 (30.59)		
Male	103 (69.59)	44 (69.84)	59 (69.41)		
Hypertension, n (%)				χ^2 = 0.10	0.750
No	118 (79.73)	51 (80.95)	67 (78.82)		
Yes	30 (20.27)	12 (19.05)	18 (21.18)		
Diabetes mellitus, n (%)				χ^2 = 0.05	0.827
No	121 (81.76)	51 (80.95)	70 (82.35)		
Yes	27 (18.24)	12 (19.05)	15 (17.65)		
ASA grading, n (%)				χ^2 = 0.46	0.500
1~2	136 (91.89)	59 (93.65)	77 (90.59)		
3	12 (8.11)	4 (6.35)	8 (9.41)		
Lauren histological classification, n (%)				χ^2 = 0.20	0.906
Intestinal type	49 (33.11)	22 (34.92)	27 (31.76)		
Mixed type	30 (20.27)	12 (19.05)	18 (21.18)		
Diffuse type	69 (46.62)	29 (46.03)	40 (47.06)		
Tumor location				–	0.277
Gastric antral cancer	79 (53.38)	39 (61.90)	40 (47.06)		
Gastric angular cancer	52 (35.14)	19 (30.16)	33 (38.82)		
Lower gastric body cancer	11 (7.43)	4 (6.35)	7 (8.24)		
Pyloric canal cancer	6 (4.05)	1 (1.59)	5 (5.88)		
TNM staging				χ^2 = 0.54	0.765
I	18 (12.16)	8 (12.70)	10 (11.76)		
II	112 (75.68)	46 (73.02)	66 (77.65)		
III	18 (12.16)	9 (14.29)	9 (10.59)		

t: t-test, Z: Mann-Whitney test, χ^2: Chi-square test, -: Fisher's exact test.

SD, standard deviation; M (Q_1, Q_3), median with interquartile range; ASA, American Society of Anesthesiologists; BMI, body mass index; TNM, Tumor Node Metastasis.

II+Braun group had a substantially higher PGR ($p < 0.001$) at T3 compared with the Billroth II group. However, no statistical difference was observed in G-17 levels at T3 between the two groups (p = 0.943). These observations indicate that Billroth II+Braun anastomosis can improve the PGR level in patients undergoing laparoscopic gastric cancer surgery, whereas its effect on G-17 appears limited.

Comparison of Postoperative Complications Between the Two Groups

As summarized in Table 4, there were no statistical differences between the two groups in terms of postoperative complications. Specifically, no substantial differences were observed in the incidence of anastomotic leakage (Fisher's exact test, p = 0.312), anastomotic stenosis (Fisher's exact test, p = 1.000), duodenal stump bleeding (Fisher's exact test, p = 0.426), duodenal stump leakage (Fisher's exact test, p = 0.180), and intestinal obstruction rate (Fisher's exact test, p = 0.402).

These findings reveal that, regarding short-term complications, Billroth II+Braun anastomosis exhibits a safety profile comparable to that of Billroth II alone in patients receiving laparoscopic gastric cancer surgery.

Assessment of Long-Term Efficacy Between the Two Study Groups

The patients were followed for 1 year after surgery through an outpatient service and telephone interviews. Long-term outcomes evaluated during follow-up primarily included bile reflux rate, reflux residual gastritis, and 1-year survival rate. As presented in Table 5, the bile reflux rate was considerably lower in the Billroth II+Braun group compared to

Table 2. Comparison of perioperative stress indicators between the two groups, Mean ± SD.

Variable	Time	Total (n = 148)	Billroth II (n = 63)	Billroth II+Braun (n = 85)	Statistic	*p*-value
CRP (mg/L)	T0	5.67 ± 0.66	5.66 ± 0.75	5.68 ± 0.59	$t = -0.16$	0.872
	T1	36.72 ± 3.63	36.88 ± 3.09	36.60 ± 4.00	$t = 0.47$	0.638
	T2	88.69 ± 31.46	83.78 ± 31.48	92.33 ± 31.12	$t = -1.64$	0.102
NE (ng/L)	T0	34.99 ± 3.67	35.55 ± 4.03	34.57 ± 3.35	$t = 1.56$	0.121
	T1	105.77 ± 14.78	104.51 ± 14.97	106.69 ± 14.66	$t = -0.89$	0.377
	T2	80.70 ± 10.44	79.78 ± 10.18	81.38 ± 10.63	$t = -0.92$	0.360
COR (µg/dL)	T0	15.85 ± 3.02	16.24 ± 2.89	15.56 ± 3.10	$t = 1.35$	0.179
	T1	31.46 ± 6.07	31.28 ± 6.13	31.59 ± 6.07	$t = -0.31$	0.755
	T2	17.52 ± 4.63	17.97 ± 4.63	17.19 ± 4.63	$t = 1.01$	0.315

t: *t*-test. CRP, C-reactive protein; NE, norepinephrine; COR, cortisol.

Table 3. Comparison of PGR and G-17 levels between the two groups, Mean ± SD.

Variable	Time	Total (n = 148)	Billroth II (n = 63)	Billroth II+Braun (n = 85)	Statistic	*p*-value
PGR	T0	4.15 ± 0.51	4.19 ± 0.53	4.12 ± 0.50	$t = 0.81$	0.419
	T3	6.51 ± 1.32	5.85 ± 1.12	7.00 ± 1.24	$t = -5.82$	$<$0.001
G-17 (pg/mL)	T0	21.92 ± 4.81	22.23 ± 4.57	21.69 ± 4.99	$t = 0.67$	0.501
	T3	11.48 ± 4.07	11.50 ± 3.99	11.46 ± 4.15	$t = 0.07$	0.943

t: *t*-test. PGR, pepsinogen I to pepsinogen II ratio; G-17, Gastrin-17.

the Billroth II group ($p = 0.005$). However, no statistically significant differences were found between the two groups regarding residual food ($p = 0.097$), reflux residual gastritis (Fisher's exact test, $p = 0.312$) or 1-year survival rate (Fisher's exact test, $p = 0.700$). These results suggest that the Billroth II+Braun anastomosis can reduce postoperative bile reflux rate after laparoscopic gastric cancer surgery.

Discussion

A major objective in radical gastrectomy for gastric cancer is to identify an optimal approach for digestive tract reconstruction. The Billroth procedure has made brilliant achievements in the surgical history of digestive tract reconstruction. Among these approaches, Billroth II anastomosis is widely used for reconstruction after distal gastrectomy because it avoids excessive anastomotic tension and is a technically simple procedure. However, by changing the normal anatomical and physiological structure of the gastrointestinal tract, the Billroth II procedure may predispose patients to postoperative function-related complications. Particularly, alkaline intestinal fluid reflux is a common concern and can significantly affect postoperative quality of life. To reduce these complications, Braun proposed in 1892 the addition of a side-to-side anastomosis between the input loop jejunum and the output loop jejunum. Although proposed more than 100 years ago, the Braun anastomosis remains one of the most frequently used and continues to be a preferred reconstruction regimen among gastrointestinal surgeons in China.

This study primarily compared the effects of Billroth II+Braun anastomosis and Billroth II anastomosis in patients undergoing laparoscopic gastric cancer surgery, focusing on perioperative stress indicators and pepsinogen-related markers. The stress response during gastric cancer surgery encompasses physiological stress caused by surgical trauma and psychological stress experienced by patients. Existing studies have confirmed that the hypothalamic-pituitary-adrenal axis plays a crucial role in mediating this response. Surgical stress induces the massive release of COR and NE into peripheral blood circulation, accompanied by increases in catecholamine and inflammatory factors, including CRP, which can inhibit cellular immune response and may lead to tumor progression and metastasis.

In our study, CRP increased gradually from T0 to T1 and T2, whereas NE and COR increased initially and then decreased. Surgical trauma causes tissue injury and necrosis, releasing a large number of inflammatory mediators such as interleukin-6 (IL-6) and tumor necrosis factor-α (TNF-α). These cytokines stimulate liver cells to synthesize and secrete CRP. Generally, postoperative CRP increases appear as a delayed response and gradually decline within 7–10 days after surgery. NE and COR are the core indicators of neuroendocrine stress response and usually reach peak levels at the end of surgery or on postoperative day 1, indicating the severe endocrine response to surgical trauma, followed by a gradual decrease. In this study, no statistical differences in CRP, NE, or COR were found between the Billroth II+Braun group and the Billroth II group at any time point. The primary reason is that, apart from the addition of the Braun anastomosis, the other operative steps were identical in both groups. Additionally, the surgical techniques for residual gastrojejunal anastomosis were also similar, and no additional tissue trauma was induced.

Table 4. Comparison of postoperative complications between the two groups, n (%).

Variable	Billroth II (n = 63)	Billroth II+Braun (n = 85)	Statistic	*p*-value
Anastomotic leakage	3 (4.76)	1 (1.18)	-	0.312
Anastomotic stenosis	1 (1.59)	1 (1.18)	-	1.000
Duodenal stump bleeding	1 (1.59)	0 (0.00)	-	0.426
Duodenal stump leakage	2 (3.17)	0 (0.00)	-	0.180
Intestinal obstruction	4 (6.35)	2 (2.35)	-	0.402

-: Fisher's exact test.

Table 5. Evaluation of long-term efficacy between the two groups, n (%).

Variable	Billroth II (n = 63)	Billroth II+Braun (n = 85)	Statistic	*p*-value
Bile reflux rate	17 (26.98)	8 (9.41)	$\chi^2 = 7.96$	0.005
Reflux residual gastritis	3 (4.76)	1 (1.18)	-	0.312
Survival rate	60 (95.24)	82 (96.47)	-	0.700
Residual food	21 (33.33)	18 (21.18)	$\chi^2 = 2.755$	0.097

χ^2: Chi-square test, -: Fisher's exact test.

In terms of gastrointestinal functional indices, Billroth II+Braun anastomosis was associated with substantially increased PGR, whereas no significant improvement was found in G-17. PGR is an indicator of gastric mucosal function and is commonly used in evaluating the risk of atrophic gastritis or gastric cancer. G-17 is primarily produced by gastric antrum G cells and is a key regulator of gastric acid secretion. Because distal gastrectomy removes the gastric antrum, a significant decrease in G-17 levels is expected postoperatively, as noted in both groups. However, this study found no difference between the two groups, indicating that the Braun anastomosis does not substantially affect gastrin regulation in the residual stomach or duodenum. After distal gastrectomy, the gastric antrum mucosa, a major source of pepsinogen II (PGII), is largely excised, whereas gastric fundus glands secreting pepsinogen I (PGI) are relatively preserved [15,16]. This anatomical alteration leads to a physiological or mechanical increase in PGR, likely reflecting altered glandular composition. However, the significantly higher postoperative PGR found in the Billroth II+Braun group may be related to the effective shunt of bile and the reduction of chemical damage of the residual gastric mucosa, possibly facilitating the preservation of functional integrity of the gastric mucosa. Further studies combining endoscopic mucosal evaluation and long-term functional follow-up are warranted to validate these findings comprehensively.

In terms of postoperative complications, duodenal stump leakage is a serious early adverse event, often occurring within 1–7 days after Billroth II or Roux-en-Y anastomosis. Failure to reinforce the duodenal stump is considered the principal risk factor. Other independent risk factors include poor nutritional status, tumor location, increased preoperative CRP levels, and postoperative intestinal obstruction. In this study, duodenal stump leakage occurred in only 2 cases in the Billroth II group. Both cases were clinically mild and significantly relieved with conservative treatment such as continuous negative-pressure drainage and anti-infective therapy. Intestinal obstruction is another adverse event observed after Billroth II anastomosis and represents a common site-specific concern after surgery. In this study, 2 cases of intestinal obstruction were found in the Billroth II+Braun group, compared with 4 cases in the Billroth II group; thus, the difference between the two anastomosis methods did not reach statistical significance.

Furthermore, delayed postoperative recovery of intestinal function was observed in some patients, manifested as impaired food transportation and even food stagnation in the intestine, resulting in excessive intestinal pressure and triggering intestinal obstruction. However, the addition of the Braun anastomosis may effectively reduce this mechanism by supporting diversion of bile into the distal small intestine, thereby alleviating intestinal pressure. Furthermore, the side-to-side anastomosis also plays a storage role to a certain extent, which can reduce food retention and improve intestinal dynamics. Although a lower incidence of postoperative intestinal obstruction was found in the Billroth II+Braun groups, the small sample size likely reduced the statistical power to identify significant differences between groups.

The primary postoperative complication after Billroth II reconstruction is the alkaline digestive juice reflux into the residual stomach, leading to secondary residual gastritis and esophagitis. This may further contribute to more severe conditions such as gastric stump carcinoma (GSC) and esophageal cancer, significantly influencing the quality of life. Yang *et al*. [17] reported that the incidence rate of bile reflux following Billroth II anastomosis may reach about 70%, with 25% of cases experiencing related clinical symptoms. A meta-analysis conducted by Jiang *et al*. [18], comparing Billroth I, Billroth II, and Roux-en-Y, reported that Billroth II anastomosis was less effective in reducing bile reflux. In our study, the bile reflux rate was substantially lower in the Billroth II+Braun group ($p = 0.005$), which is consistent with the results reported by Yalikun *et al*. [19]. These findings indicate that the addition of Braun anastomosis can reduce the risk of bile reflux-related complications to a certain extent.

Despite several promising findings, this study has several limitations that should be considered before interpreting these outcomes: (1) This is a single-center study with a relatively small sample size, and the follow-up is limited to only 1 year after surgery. These factors may limit the generalizability of the results. Future multi-center studies with a large sample size are needed to further validate the clinical effectiveness and long-term outcomes of Billroth II+Braun anastomosis. (2) The retrospective study design introduces some inherent limitations. The process of case selection and data extraction may have been affected by the subjective judgment of the researchers, which can potentially elevate the risk of selection bias and information bias. (3) Due to the limited number of eligible patients, certain postoperative adverse events were observed at low frequencies, making statistical comparison less powerful. The small number of complications may have decreased the power to identify considerable differences between the two groups.

Conclusions

Billroth II+Braun anastomosis and Billroth II anastomosis have their distinct advantages and disadvantages and have a potential role in clinical practice. The frequency of postoperative complications remains a crucial factor affecting the long-term quality of life. Billroth II+Braun anastomosis can improve PGR level and reduce bile reflux rate. In clinical decision-making, clinicians should adhere to the basic oncologic and surgical principles, considering tumor stage and overall physical condition. A thorough preoperative evaluation is warranted to guide the choice of an appropriate and standardized treatment regimen.

Availability of Data and Materials

The data used and analyzed during the current study are available from the corresponding author on reasonable request.

Author Contributions

HTS contributed to the conception and design, data acquisition, data analysis, and the writing of the manuscript. YMY and YDW contributed to the collection and organization of the data. BL and BZZ contributed to the data analysis. CHH and YZ contributed to the data interpretation and manuscript review and revision. All authors revised the manuscript critically for important intellectual content. All authors gave final approval of the version to be published. All authors have participated sufficiently in the work to take public responsibility for appropriate portions of the content and agreed to be accountable for all aspects of the work in ensuring that questions related to its accuracy or integrity.

Ethics Approval and Consent to Participate

This study was approved by the medical ethics committee of The Second Affiliated Hospital of Jiaxing University (Approval No. 2025-019). Informed consent was obtained from all patients, and the study was conducted in accordance with the principles of the Declaration of Helsinki.

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Conflict of Interest

The authors declare no conflict of interest.

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